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ABSTRACT

The availability of an increased variety of therapeutic approaches provides the opportunity to improve hypertension control while minimizing adverse effects that may influence cardiovascular complications and adherence to therapy. This report serves two purposes: (1) to guide practicing physicians and other health professionals in their care of hypertensive patients; and (2) to guide health professionals participating in the many community high blood pressure control programs. Contents include: (1) definition and prevalence of high blood pressure; (2) detection, confirmation and referral; (3) evaluation and diagnosis; (4) treatment--nonpharmacologic and pharmacologic therapy, and long-term maintenance of therapy; (5) considerations in individual therapy; and (6) special populations and management problems. Fifty-five references are included. (JD)

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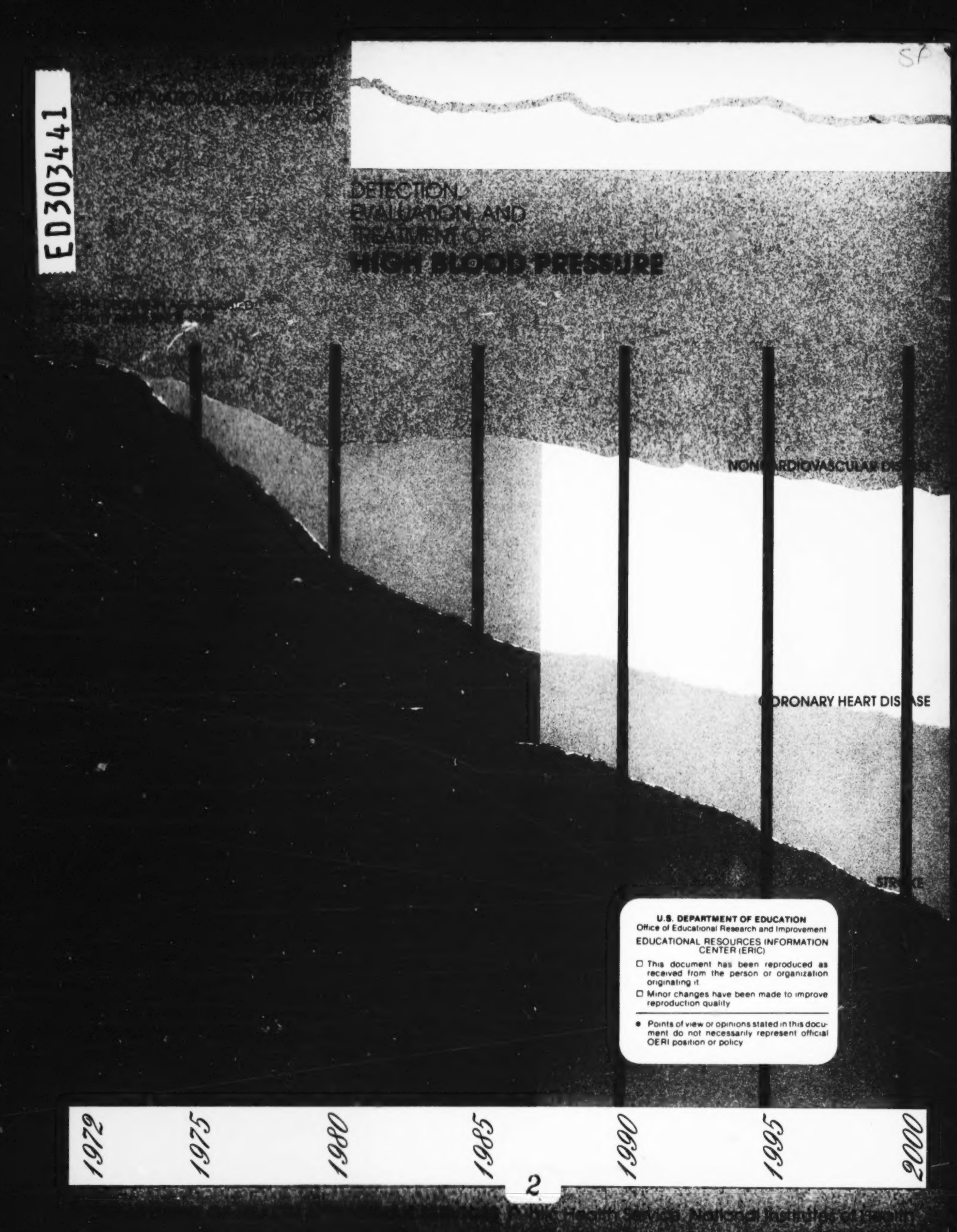
JOINT NATIONAL COMMITTEE

DETECTION, EVALUATION, AND TREATMENT OF HIGH BLOOD PRESSURE



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The 1988 Report of the Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure

National High Blood Pressure Education Program
National, Heart, Lung, and Blood Institute

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
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National Institutes of Health

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Foreword

Since 1972, the National High Blood Pressure Education Program (NHBPEP) has released three Joint National Committee reports plus a task force report on the detection, evaluation, and treatment of high blood pressure. Each report was based on the latest scientific research related to hypertension control and reflected the state of the art regarding hypertension management. Through the years, application of updated research results has contributed to the prevention of heart attacks, kidney disease, and strokes in the United States.

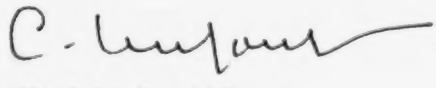
Today, the management of hypertension is different than when the NHBPEP began in 1972. Clinical trial data, epidemiological studies, drug studies, and basic research on the mechanisms of hypertension provide new exciting knowledge on controlling this disease. With this increase in knowledge and information come different interpretations on how to handle these complex issues. The need for consensus becomes even greater, but admittedly it becomes more difficult. It is recognized that consensus provides a way that most agree will benefit the majority of patients.

The 1988 Joint National Committee members are to be congratulated for accepting and meeting a formidable challenge—to review previous NHBPEP documents and the latest scientific research and then produce a concise report that will help practitioners manage this highly prevalent disease. Under the stellar leadership of Dr. Aram Chobanian, the committee expeditiously developed a splendid document. The new document:

- broadens the step-care approach to provide more flexibility for clinicians;
- encourages greater involvement of the patient in the treatment program;
- addresses the quality of life in the management of patients;
- provides a discussion on the cost of care;
- provides more emphasis on control of other cardiovascular disease risk factors and includes discussion of the new cholesterol guidelines;
- recommends a reduction in alcohol consumption;
- discusses the use of calcium and fish oil supplementation;
- examines the needs of special populations, including blacks and other racial and ethnic minority groups, young and elderly patients, pregnant patients, surgical candidates, and hypertensives with coexisting medical conditions (i.e., cerebrovascular disease, coronary artery disease, left ventricular hypertrophy, congestive heart failure, peripheral vascular disease, chronic obstructive pulmonary disease, asthma, gout, diabetes mellitus, and hyperlipidemia);

- updates previous drug tables to include new drugs, revised recommended doses, and drug interactions;
- suggests consideration of step-down therapy after blood pressure has been controlled; and
- summarizes recent clinical trial data and provides implications of this information for medical practitioners.

I am pleased to recommend this report to health care practitioners. It is evidence of what can be done when national leaders work together to resolve important public health problems.



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High Blood Pressure

Introduction

Since publication of the first report of the Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure, remarkable changes have occurred in the control of hypertension. The public is more knowledgeable about high blood pressure, more likely to visit a physician for hypertension, and more likely to follow medical advice. These practices have led to impressive gains in hypertension control and have contributed to the 50-percent decline in the national age-adjusted stroke mortality rate since 1972. During this time period, there has also been a 35-percent decline in coronary artery disease mortality.

If this progress is to continue, a number of events must occur. The hypertension control process must be extended to the entire population, and aggressive treatment must also take into consideration the lifestyles and concomitant conditions of individual patients. The availability of an increased variety of therapeutic approaches provides the opportunity to improve hypertension control while minimizing adverse effects that may influence cardiovascular complications and adherence to therapy.

Purpose of the Report

This report serves two purposes:

- to guide practicing physicians and other health professionals in their care of hypertensive patients; and
- to guide health professionals participating in the many community high blood pressure control programs.

The National High Blood Pressure Education Program (NHBPEP) Coordinating Committee anticipates the release of additional publications that will expand on the guidelines presented herein.

High Blood Pressure

Definition and Prevalence of High Blood Pressure

As many as 58 million people in the United States have elevated blood pressure (systolic blood pressure ≥140 mm Hg and/or diastolic blood pressure ≥ 90 mm Hg) or are taking antihypertensive medication. The prevalence rate of hypertension increases with age and is higher in blacks than in whites.[1] Regional variations in blood pressure have also been observed. For example, blacks in the southeastern United States have a greater prevalence rate and severity of hypertension as well as a greater stroke death rate than do blacks in other areas of the country.

Risk of cardiovascular complications related to hypertension increases continuously with increasing levels of both systolic blood pressure (SBP) and diastolic blood pressure (DBP). Table 1 provides a categorical scheme based on risk level for classification of systolic and diastolic blood pressure for persons age 18 years and older. High normal blood pressure is included as a category for monitoring purposes. In this classification scheme, the term "mild" is relative to the other categories and should not be interpreted to patients as unimportant. Data from clinical trials have indicated that mild hypertension requires medical attention.

Table 1 Classification of Blood Pressure# in Adults Age 18 Years or Older

Range, mm Hg	Category*
Diastolic	
< 85	Normal blood pressure
85-89	High normal blood pressure
90-104	Mild hypertension
105-114	Moderate hypertension
≥ 115	Severe hypertension
Systolic, when diastolic blood pressure is <90	
< 140	Normal blood pressure
140-159	Borderline isolated systolic hypertension
≥ 160	Isolated systolic hypertension

Classification based on the average of two or more readings on two or more occasions.

* A classification of borderline isolated systolic hypertension (SBP 140 to 159 mm Hg) or isolated systolic hypertension (SBP ≥160 mm Hg) takes precedence over high normal blood pressure (diastolic blood pressure, 85 to 89 mm Hg) when both occur in the same person. High normal blood pressure (DBP 85 to 89 mm Hg) takes precedence over a classification of normal blood pressure (SBP <140 mm Hg) when both occur in the same person.

Detection, Confirmation, and Referral

Hypertension control begins with detection and requires continued surveillance. Health care professionals are strongly encouraged to measure blood pressure at each patient visit. Most adults already know their blood pressure value or have had it measured. Although active detection efforts should continue, mass screening programs for this purpose are now seldom indicated. Rather, resources should be concentrated primarily on the following: controlling blood pressure in those persons already identified as having hypertension; detecting those groups at high risk of developing hypertension; and contacting those with limited access to the health care system. Wherever blood pressure measurements are obtained, the following guidelines are recommended for identifying persons at risk and bringing them under continuing medical care.

Measurement

Hypertension should not be diagnosed on the basis of a single measurement. Initial elevated readings should be confirmed on at least two subsequent visits, with average levels of diastolic pressure of 90 mm Hg or greater or systolic pressure of 140 mm Hg or greater required for diagnosis.

Since blood pressure is variable and can be affected by multiple extraneous factors, it should be measured in such a manner that the values obtained are representative of patients' usual level.[2] The following techniques are strongly recommended.

- Patients should be seated with their arm bared, supported, and positioned at heart level. They should not have smoked or ingested caffeine within 30 minutes prior to measurement.
- Measurement should begin after 5 minutes of quiet rest.
- The appropriate cuff size must be used to ensure an accurate measurement. The rubber bladder should encircle at least two-thirds of the arm. Several sizes of cuffs (e.g., child, adult, and large adult) should be available.
- Measurements should be taken with a mercury sphygmomanometer, a recently calibrated aneroid manometer, or a validated electronic device.
- Both systolic and diastolic pressures should be recorded. The disappearance of sound (phase V) should be used for the diastolic reading.
- Two or more readings should be averaged. If the first two readings differ by more than 5 mm Hg, additional readings should be obtained.

Patients should be informed of their blood pressure reading and advised of the need for periodic remeasurement. Table 2 provides follow-up advice based on the initial blood pressure measurement.

Table 2 Follow-Up Criteria for Initial Blood Pressure Measurement for Adults Age 18 Years or Older

Range, mm Hg	Recommended Follow-Up*
Diastolic	
< 85	Recheck within 2 years
85-89	Recheck within 1 year
90-104	Confirm within 2 months
105-114	Evaluate or refer promptly to source of care within 2 weeks
≥ 115	Evaluate or refer immediately to source of care
Systolic, when diastolic blood pressure is <90	
< 140	Recheck within 2 years
140-199	Confirm within 2 months
≥ 200	Evaluate or refer promptly to source of care within 2 weeks

* If recommendations for follow-up of diastolic and systolic blood pressure are different, the shorter recommended time for recheck and referral should take precedence.

Confirmation and Follow-Up

Repeated blood pressure measurements will determine whether initial elevations persist and require close observation or prompt attention, or whether they have returned to normal and need only periodic remeasurement. Initial blood pressure readings that are markedly elevated (i.e., DBP ≥ 115 mm Hg) or associated with evidence of target organ damage may require immediate drug therapy. The timing of subsequent readings should be based on the initial blood pressure level (Table 2). In mild hypertensives, observation over a 3- to 6-month interval may be elected prior to initiating drug therapy since pressures may return to normal during that time. Individuals with such temporary elevations of pressure are at increased risk of later developing persistent hypertension and should be informed of this and observed at approximately 6-month intervals.

As an adjunct to repeated office readings, blood pressure may be measured at the worksite or at home by patients (or a friend or family member), provided they are instructed in proper measurement techniques. A standard cuff with sphygmomanometer is generally the most practical instrument. Automatic and semiautomatic devices using acoustic or oscillometric methods and digital display of readings are acceptable for home use, provided that the manufacturer has documented the validity and reliability of the unit and that it is periodically calibrated and maintained.[3]

Twenty-four-hour ambulatory blood pressure devices are currently available, but such ambulatory monitoring is not recommended for diagnosis and follow-up of the majority of hypertensive patients.[3] In a few patients (e.g., those in whom therapeutic decisions may be difficult because of marked lability in blood pressure), 24-hour monitoring may be of value. However, the technique is not usually cost-effective.

Evaluation and Diagnosis

Clinical evaluation of patients with confirmed hypertension should help answer the following questions: (1) Does the patient have primary or secondary (possibly reversible) hypertension? (2) Is target organ involvement present? (3) Are cardiovascular risk factors other than high blood pressure present?

Medical History

A medical history should include the following:

- family history of high blood pressure and cardiovascular disease;
- patient history of cardiovascular, cerebrovascular, and renal disease as well as diabetes mellitus;
- known duration and levels of elevated blood pressure;
- results and side effects of previous antihypertensive therapy;
- history of weight gain, exercise activities, sodium intake, fat intake, and alcohol use;
- symptoms suggesting secondary hypertension;
- psychosocial and environmental factors (e.g., emotional stress, cultural food practices, and socioeconomic status) that may influence blood pressure control; and
- other cardiovascular risk factors (including obesity, smoking, hyperlipidemia, and carbohydrate intolerance).

Health practitioners should obtain a history of all prescribed and over-the-counter medications from all patients. Several medications may either raise blood pressure or interfere with the effectiveness of antihypertensive drugs. These drugs include, but are not limited to, oral contraceptives, steroids, nonsteroidal anti-inflammatory agents, nasal decongestants and other cold remedies, appetite suppressants, cyclosporin, tricyclic antidepressants, and monoamine oxidase inhibitors.

Physical Examination

The initial physical examination should include the following:

- two or more blood pressure measurements with the patient standing and either supine or seated;
- verification in the contralateral arm (if values are discrepant, the higher value should be used);
- measurement of height and weight;
- funduscopic examination for arteriolar narrowing, arteriovenous compression, hemorrhages, exudates, and papilledema;
- examination of the neck for carotid bruits, distended veins, and an enlarged thyroid gland;

- examination of the heart for increased rate, increased size, precordial heave, clicks, murmurs, arrhythmias, and S_3 and S_4 heart sounds;
- examination of the abdomen for bruits, enlarged kidneys, masses, and dilation of the aorta;
- examination of the extremities for diminished or absent peripheral arterial pulsations, bruits, and edema; and
- neurologic assessment.

Secondary hypertension is rare; nevertheless, examination should seek to eliminate this possibility. Physical findings that are suggestive of secondary hypertension include abdominal or flank masses (polycystic kidneys); abdominal bruits, particularly those that lateralize or have a diastolic component (renovascular disease);[4] delayed or absent femoral arterial pulses or decreased blood pressure in lower extremities (aortic coarctation); truncal obesity with pigmented striae (Cushing's syndrome); and tachycardia, orthostatic hypotension, sweating, and pallor (pheochromocytoma). Additional diagnostic procedures may be indicated to discover causes of secondary hypertension, particularly in patients: (1) in whom age, history, physical examination, severity of hypertension, or initial laboratory findings suggest secondary hypertension; (2) whose blood pressures are responding poorly to drug therapy; (3) with well-controlled hypertension whose blood pressures begin to increase; and (4) with accelerated or malignant hypertension.

Laboratory Tests

A few simple laboratory tests should be performed before initiating therapy. These include determination of hemoglobin and hematocrit values; complete urinalysis; measurement of serum potassium, calcium, and creatinine levels; electrocardiography; and measurement of total and high-density lipoprotein plasma cholesterol (if abnormal, plasma triglycerides and calculated low-density lipoprotein levels), plasma glucose (fasting, if possible), and serum uric acid concentrations.

Some of these tests are needed to determine severity of cardiovascular disease and possible causes of hypertension. The remainder relate to other cardiovascular risk factors or provide baseline values for judging biochemical effects of therapy.

Opinions differ regarding risks and specificity of some diagnostic procedures. An automated battery of blood chemistry tests is often used to minimize costs. Physicians may select additional tests based on their clinical judgment. Type and frequency of repeated laboratory tests should be based on the severity of target organ damage and the effects of the selected treatment program.

Treatment

The goal of treating patients with hypertension is to prevent morbidity and mortality associated with high blood pressure. The objective is to achieve and maintain arterial blood pressure below 140/90 mm Hg, if possible.

Although numerous multicenter clinical trials have demonstrated the benefits of therapy, the decision to initiate treatment in individual patients requires physicians to consider at least two factors: the severity of blood pressure elevation and the presence of other complications. The effectiveness of antihypertensive drugs in reducing elevated arterial pressure is well established. In this regard, recent evidence suggests that nonpharmacologic approaches—particularly weight reduction, salt restriction, and moderation of alcohol consumption—may lower elevated pressure and improve the efficacy of pharmacologic agents. Therefore, nonpharmacologic approaches are used both as definitive intervention and as an adjunct to pharmacologic therapy and should be considered for all antihypertensive therapy.[5] Clinicians may wish to refer to other health providers for specific counseling related to lifestyle changes.

Nonpharmacologic Therapy

Some of the following nonpharmacologic therapies are recommended for hypertension control. The remainder are included to reduce other cardiovascular risk factors.

Weight Reduction

As shown by worldwide epidemiologic studies, obesity and blood pressure are closely associated. Moreover, a strong correlation exists between body weight and blood pressure and between increases in body weight and subsequent development of hypertension.[6] Weight reduction may reduce arterial pressure in overweight hypertensives; this fall in pressure may occur with caloric restriction alone, even without reduction in sodium intake and before ideal body weight is achieved.

Because of the clear relationship between obesity and blood pressure, all obese hypertensive adults should participate in weight reduction programs, with goal body weight being within 15 percent of desirable weight. Concomitantly, health professionals should vigorously promote weight control, particularly for those at increased risk of becoming hypertensive because of a family history of this condition. These recommendations are made with the clear recognition that weight reduction is difficult to achieve and that the rate of recidivism is high.

Restriction of Alcohol

Excess alcohol intake may lead to elevated blood pressure, poor adherence to antihypertensive therapy, and, occasionally, refractory hypertension.[7] Therefore, for controlling hypertension, those who drink should do so in moderation (i.e., no more than 1 ounce of ethanol daily). One ounce of ethanol is contained in 2 ounces of 100-proof whiskey, approximately 8 ounces of wine, or 24 ounces of beer.

Restriction of Sodium

A high sodium intake plays a critical role in maintaining the elevated blood pressure of some hypertensive patients and in limiting the effectiveness of certain antihypertensive drugs. Moreover, some patients with mild or moderate blood pressure elevation may achieve control through moderate sodium restriction to 70 to 100 mEq per day (i.e., approximately 1.5 to 2.5 grams of sodium or 4 to 6 grams of salt). There is no easy way to identify those patients who will benefit from sodium restriction.[8] Although the effect of sodium restriction on individual patients cannot be predicted, this degree of limitation produces no serious adverse consequences. Since much of daily sodium intake comes from prepared foods,[9] merely refraining from adding salt at the table is usually inadequate to control hypertension. Thus, proper counseling is necessary to achieve moderate sodium restriction. This counseling should include reference to sodium labeling of canned, frozen, and other processed foods, both to reduce sodium intake and to maintain adequate overall nutrition.

Role of Other Cations

Data have suggested that reduced potassium intake may be associated with high blood pressure[10] and that high potassium intake (i.e., greater than 80 mEq or 3 to 4 grams per day) has a modest blood-pressure-lowering effect.[11] The evidence in this regard is still developing, and if increased potassium intake is recommended, it should be restricted to those patients who have normal renal function and who are not taking drugs known to raise serum potassium levels, such as potassium-sparing diuretics and angiotensin-converting enzyme (ACE) inhibitors.

Increased intake of calcium has been reported to lower blood pressure in some individuals.[12] However, some studies have suggested that a direct relationship exists between serum calcium concentration and blood pressure.[13] It is still not known which patients will benefit from dietary calcium supplementation. Moreover, the risk for developing renal calculi may become greater with increased dietary calcium. The data concerning calcium appear inadequate at this time to warrant specific recommendations. Similarly, the evidence regarding magnesium, zinc, and lead is too meager to justify any recommendations.

Tobacco Avoidance

Although nicotine may increase arterial blood pressure acutely, prolonged use is not associated with an increased prevalence of hypertension. However, individuals who smoke definitely increase their risk for cancer and pulmonary diseases and, overall, more than double their cardiovascular risk for coronary artery disease and sudden death.[14,15] Smokers appear to have a higher frequency of malignant hypertension[16] and subarachnoid hemorrhage.[17] In addition, studies have shown an interaction between propranolol hydrochloride and smoking in which smokers require larger doses of this drug to achieve reductions in blood pressure similar to those attained by nonsmokers. Furthermore, risk reduction induced by antihypertensive therapy may not be as great in smokers as in nonsmokers.[18]

The benefits of tobacco avoidance have been proven conclusively, and smoking cessation is strongly recommended. A key component of every therapeutic regimen for hypertension should include counseling to help patients stop smoking.[19]

Biofeedback and Relaxation

Recent data concerning behavioral approaches to hypertension management have demonstrated that various relaxation and biofeedback therapies produce modest long-term reductions in blood pressure in selected groups.[20,21] These studies have suggested that combining biofeedback and relaxation procedures may produce better therapeutic results than either approach alone.[22] Such regimens are most useful for the treatment of mild hypertension and may also be used in combination with pharmacologic therapy. These promising methods have yet to be subjected to rigorous clinical trial evaluation and should not be considered as definitive treatment for patients with high blood pressure.

Exercise

A regular aerobic exercise program (e.g., walking, bicycling, jogging, or swimming) facilitates weight control and may be helpful in reducing blood pressure. Health practitioners should advise hypertensive patients who are initiating an exercise program to do so gradually and after appropriate clinical evaluation.

Modification of Dietary Fats

Some studies have suggested that low intake of saturated fat and high intake of polyunsaturated fat are associated with lower arterial blood pressure;[23] others have not demonstrated this effect.[24] The evidence is still inadequate to recommend such dietary changes for hypertension control, but these modifications could be important for lowering blood cholesterol and reducing risk of developing coronary artery disease.

Public attention has focused recently on the value of fish and fish oils in the diet as a result of observations that populations eating large amounts of fish have lower rates of coronary artery disease. Eating fish that are rich in the polyunsaturated omega-3 fatty acids may lower blood levels of triglycerides. However, fish oil supplementation can interfere with the ability of blood to clot and, in some individuals, may cause excessive bleeding. Therefore, while fish consumption is recommended, the health benefits of fish oil capsules have not been proven.

Pharmacologic Therapy

Efficacy

Reduction of blood pressure with drugs clearly decreases cardiovascular mortality and morbidity in patients with diastolic blood pressure greater than 104 mm Hg.[25] In patients with mild hypertension (DBP 90-104 mm Hg), trials of antihypertensive therapy have shown protection against stroke, congestive heart failure, progression to more severe levels of hypertension, and all-cause mortality.[25-28] A 30- to 50-percent reduction in both fatal and nonfatal strokes with therapy has been demonstrated.

These clinical trials usually involved diuretics as initial therapy, although the Medical Research Council (MRC) trial did include a propranolol-treated group.[28] Clinical trials have not yet produced long-term data on the effects of alpha-blockers, ACE inhibitors, or calcium antagonists on cardiovascular complications and mortality in hypertensive patients.

Protection against the complications of coronary artery disease as a result of antihypertensive therapy has not been convincingly demonstrated. A summary analysis of nine clinical trials shows a trend of reduced mortality from coronary artery disease in the intervention groups, but the difference does not reach statistical significance.[29] Many explanations have been proposed for the lack of demonstrated benefit for coronary artery disease, including: (1) multifactorial causes of coronary artery disease and the failure to reduce other risk factors; (2) reduction of perfusion to below a critical level in the coronary circulation by lowering blood pressure in those individuals with preexisting coronary artery disease;[30] (3) insufficient sample size, inadequate duration of clinical trials to detect favorable changes, and inappropriate type of population studied; (4) undesired effects of the antihypertensive drugs causing increased coronary risk; and (5) initiation of studies too late in the natural course of hypertension. However, it is unknown whether these explanations account for the inability of studies to demonstrate significant effects of therapy on the incidence of coronary artery disease.

Mild Hypertension

Selection of patients for drug treatment. The benefits of drug therapy appear to outweigh any known risks to individuals with a persistently elevated diastolic pressure greater than 94 mm Hg and to those with lesser elevations who are otherwise at high risk (e.g., men; smokers; or patients with target organ damage, diabetes mellitus, hyperlipidemia, or other major risk factors for cardiovascular disease). Data from the 1976-1980 National Health and Nutrition Examination Survey (NHANES II) indicate that approximately 58 percent of the individuals (age 20-74 years) with diastolic pressures 90 to 94 mm Hg also have one or more of the following conditions: smoking, self-reported diabetes, or serum cholesterol levels $\geq$ 240 mg/dL.[31]

Patients whose diastolic pressures fall between 90 and 94 mm Hg and who are otherwise at relatively low risk of developing cardiovascular disease should be treated with nonpharmacologic approaches. Some experts believe that drug therapy should be initiated in these patients if diastolic pressure remains above 90 mm Hg despite vigorous attempts with nonpharmacologic approaches. Physicians who elect not to use drug therapy for patients in the range of 90-94 mm Hg should monitor their patients closely, since some will progress to higher levels of blood pressure that clearly warrant antihypertensive drug therapy.

Selection of drug treatment for uncomplicated hypertension. Several classes of antihypertensive drugs are currently available (Table 3). All have demonstrated antihypertensive efficacy, although individual patients may respond better to one drug than to another. About one-half of patients with mild hypertension will respond to a moderate dose of any one of several antihypertensive drugs by achieving a DBP reduction of 10 mm Hg or more or by lowering the diastolic pressure to the desired goal (i.e., below 90 mm Hg).

Table 3 Antihypertensive Drugs

Type of Drug	DOSAGE RANGE (mg/day)* Usual Minimum	Usual Maximum
Diuretics		
Thiazides and related sulfonamide diuretics		
Bendroflumethiazide	2.5	5
Benzthiazide	12.5-25	50
Chlorothiazide	125-250	500
Chlorthalidone	12.5-25	50
Cyclothiazide	1	2
Hydrochlorothiazide	12.5-25	50
Hydroflumethiazide	12.5-25	50
Indapamide	2.5	5
Methyclothiazide	2.5	5
Metolazone	1.25	10
Polythiazide	2	4
Quinethazone	25	100
Trichlormethiazide	1-2	4
Loop diuretics§		
Bumetanide#	0.5	5
Ethacrynic acid#	25	100
Furosemide#	20-40	320
Potassium-sparing agents		
Amiloride	5	10
Spironolactone	25	100
Triamterene	50	150

Table 3
(continued)

Type of Drug	DOSAGE RANGE (mg/day)* Usual Minimum	Usual Maximum
Adrenergic inhibitors		
Beta-adrenergic blockers[@]		
Acebutolol	200	1200
Atenolol	25	150
Metoprolol	50	200
Nadolol	40	320
Penbutolol sulfate	20	80
Pindolol[#]	10	60
Propranolol hydrochloride[#]	40	320
Propranolol, long-acting	60	320
Timolol[#]	20	80
Centrally acting alpha-blockers		
Clonidine[#]	0.1	1.2
Clonidine TTS (patch)***	0.1	0.3
Guanabenz[#]	4	64
Guanfacine hydrochloride	1	3
Methyldopa[#]	250	2000
Peripheral-acting adrenergic antagonists		
Guanadrel sulfate[#]	10	100
Guanethidine monosulfate	10	150
Rauwolfia alkaloids		
Rauwolfia (whole root)	50	100
Reserpine	0.1	0.25
Alpha-1-adrenergic blockers		
Prazosin hydrochloride[#]	1-2	20
Terazosin hydrochloride	1-2	20
Combined alpha- and beta-adrenergic blockers		
Labetalol[#]	200	1800

Table 3
(continued)

Type of Drug	DOSAGE RANGE (mg/day)* Usual Minimum	Usual Maximum
Vasodilators		
Hydralazine#	50	300
Minoxidil#	2.5	80
ACE inhibitors		
Captopril#	25-50	300
Enalapril maleate	2.5-5	40
Lisinopril	5	40
Calcium antagonists		
Diltiazem hydrochloride**	60	360
Nifedipine**	30	180
Nitrendipine	5	40
Verapamil**	120	480
Verapamil SR (long-acting)	120	480

* The dosage range may differ slightly from the recommended dosage in *Physicians' Desk Reference* or package insert.

\# This drug is usually given in divided doses twice daily.

@ Atenolol, metoprolol, and acebutolol are cardioselective; pindolol and acebutolol have partial agonist activity.

** This drug is usually given in divided doses three or four times daily.

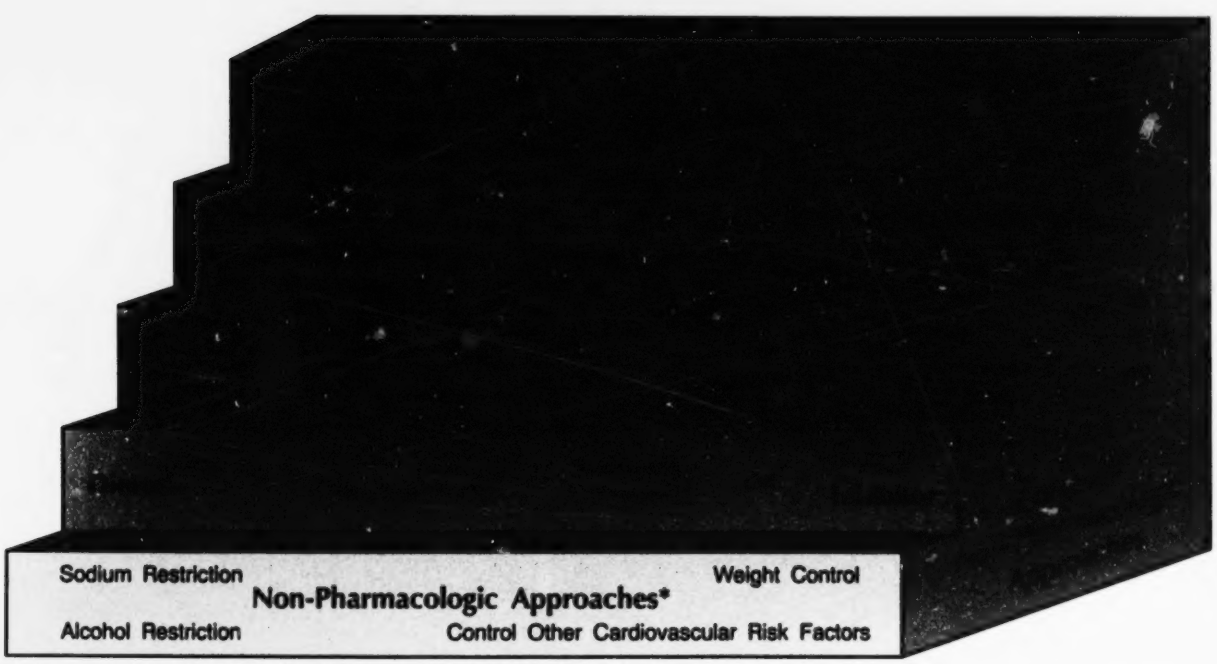
*** This drug is administered as a skin patch once weekly.

§ Larger doses of loop diuretics may be required in patients with renal failure.

Initial Drug Therapy

The 1984 Report of the Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure[32] recommended that either thiazide-type diuretics or beta-blockers be used as initial therapy, unless contraindications exist. Clinical experience obtained since then indicates that ACE inhibitors and calcium antagonists are also useful drugs for this purpose. Figure 1 illustrates a scheme for individualized step-care therapy. Some drugs, such as the direct-acting vasodilators (e.g., hydralazine and minoxidil) are not well suited for initial monotherapy since they often induce reflex sympathetic stimulation and fluid retention. However, the large numbers of effective antihypertensive drugs provide many excellent therapeutic options for lowering blood pressure effectively and minimizing side effects.

Figure 1:
Individualized Step-Care Therapy for Hypertension



* For some patients, non-pharmacologic therapy should be tried first. If goal blood pressure is not achieved, add pharmacologic therapy. Other patients may require pharmacologic therapy as initial treatment. In these instances, non-pharmacologic treatment may be a helpful adjunct.

Subsequent Therapy

If, after a 1- to 3-month interval, the response to the initial choice of therapy is inadequate, the patient is not experiencing significant side effects, and adherence to therapy is adequate, three options for subsequent therapy should be considered (Figure 1):

- increase the dose of the first drug if it is below the maximum recommended;
- add an agent from another class; or
- discontinue the initial choice, and substitute a drug from another class.

Combining antihypertensive drugs with different modes of action using the step-care approach will often allow small doses of drugs to be used to achieve control, thereby minimizing the potential for dose-dependent side effects. If a diuretic is not chosen as the first drug, it will often be required as the second one since fluid retention (pseudotolerance) may be responsible in part for the suboptimal response to non-diuretic agents and since the addition of a diuretic will usually enhance the effects of other drugs. When additional drugs are added and the combination succeeds, a later attempt should be made to reduce the dose and, if possible, to eliminate the initial drug.

Before proceeding to each successive treatment step, physicians should address possible reasons for lack of responsiveness, including those listed in Table 4.

After blood pressure is reduced to goal level and maintenance doses of antihypertensive drugs are stabilized, substituting comparable combination tablets may simplify patients' regimens, reduce medication costs, and promote adherence to a comprehensive antihypertensive treatment program.

Table 4 Causes of Refractory Hypertension

1. Nonadherence to therapy

2. Drug-related causes
   a. Doses too low
   b. Inappropriate combinations (e.g., two centrally acting adrenergic inhibitors)
   c. Rapid inactivation (e.g., hydralazine)
   d. Effects of other drugs
      (1) Sympathomimetics
      (2) Antidepressants
      (3) Adrenal steroids
      (4) Nonsteroidal anti-inflammatory drugs
      (5) Nasal decongestants
      (6) Oral contraceptives

3. Associated conditions
   a. Increasing obesity
   b. Alcohol intake more than 1 ounce of ethanol a day
   c. Renal insufficiency
   d. Renovascular hypertension
   e. Malignant or accelerated hypertension
   f. Other causes of hypertension

4. Volume overload
   a. Inadequate diuretic therapy
   b. Excess sodium intake
   c. Fluid retention from reduction of blood pressure
   d. Progressive renal damage

Step-Down Therapy and Drug Withdrawal

For patients with mild hypertension who have satisfactorily controlled their blood pressure through treatment for at least 1 year, antihypertensive drugs may be reduced in a stepwise fashion. Reduction may be particularly effective in patients who are also following nonpharmacologic therapeutic recommendations. In a study in which medications were discontinued and patients received no nutritional counseling, most cases eventually required reinitiation of drug therapy.[33] Since the goal of therapy is to control blood pressure with the fewest drugs at their lowest dose, sound patient management should include attempts to decrease the dosage or number of antihypertensive drugs while maintaining nonpharmacologic modalities. Regular follow-up must be maintained because blood pressure can rise again to hypertensive levels, even after years without therapy.

Special Considerations

Other factors should be considered in the selection of initial therapy, particularly in those patients with mild or uncomplicated hypertension who are likely to require only one drug.

- *Demographics.* Blacks and older patients tend to respond better to diuretics or calcium antagonists than to beta-blockers or ACE inhibitors. Gender has not been found to be a significant determinant of the response to drugs.
- *Concomitant diseases and therapies.* Antihypertensive drugs may worsen some diseases while improving other conditions. They also may interact with medications used to treat these problems, as shown in Table 5. For example, beta-blockers may worsen asthma and peripheral arterial disease, but they may improve angina pectoris, certain cardiac dysrhythmias, and migraine headaches. Awareness of the more common side effects of the various agents, listed in Table 6, is necessary to select drugs that may improve concomitant diseases or symptoms and to avoid those that may worsen them.
- *Lifestyle.* Antihypertensive drugs may cause undesirable symptoms. For example, many of these agents may impair sexual function; centrally acting drugs may impair mental acuity; and beta-blockers may reduce exercise tolerance.
- *Physiologic and biochemical measurements.* Some health practitioners have found certain physiologic and biochemical measurements (e.g., body weight, heart rate, plasma renin activity, resting electrocardiographic tracing, and hemodynamic functions) to be helpful in choosing specific therapy.
- *Economic considerations.* The cost of therapy may be a barrier to controlling hypertension. Treatment costs include not only the price of drugs, but also the expense of laboratory tests, supplemental therapies, office visits, and time lost from work for visits to physicians' offices.[34]

Tranquilizers and sedatives are not effective in lowering blood pressure and should not be considered for use as antihypertensive therapy.

Table 5 Drug Interactions in Anti-hypertensive Therapy

Diuretics

a. Diuretics can raise lithium blood levels by enhancing proximal tubular reabsorption of lithium.

b. Nonsteroidal anti-inflammatory agents, including aspirin, may antagonize the antihypertensive and natriuretic effectiveness of diuretics.

c. ACE inhibitors magnify potassium-sparing effects of triamterene, amiloride, or spironolactone.

d. ACE inhibitors blunt hypokalemia induced by thiazide diuretics.

Sympatholytic Agents

a. Guanethidine monosulfate and guanadrel sulfate: Ephedrine and amphetamine displace guanethidine and guanadrel from storage vesicles. Tricyclic antidepressants inhibit uptake of guanethidine and guanadrel into these vesicles. Cocaine may inhibit the neuronal pump that actively transports guanethidine and guanadrel into nerve endings. These actions may reduce the antihypertensive effects of guanethidine and guanadrel.

b. Hypertension can occur with concomitant therapy with phenothiazines or sympathomimetic amines.

c. Monoamine oxidase inhibitors may prevent degradation and metabolism of released norepinephrine produced by tyramine-containing foods and may thereby cause hypertension.

d. Tricyclic antidepressant drugs may reduce the effects of clonidine and guanabenz.

Table 5
(continued)

Beta-Blockers

a. Cimetidine may reduce the bioavailability of those beta-blockers metabolized primarily by the liver by inducing hepatic oxidative enzymes. Hydralazine, by reducing hepatic blood flow, may increase the plasma concentration of beta-blockers.

b. Cholesterol-binding resins (i.e., cholestyramine and colestipol) may reduce plasma levels of propranolol hydrochloride.

c. Beta-blockers may reduce the plasma clearance of drugs that are metabolized by the liver (e.g., lidocaine, chlorpromazine, and coumarin).

d. Combinations of calcium channel blockers and beta-blockers may promote negative inotropic effects on the failing myocardium.

e. Combinations of beta-blockers and reserpine may cause marked bradycardia and syncope.

ACE Inhibitors

a. Nonsteroidal anti-inflammatory drugs, including aspirin, may magnify the potassium-retaining effects of ACE inhibitors.

Calcium Antagonists

a. Combinations of calcium antagonists with quinidine may induce hypotension, particularly in patients with idiopathic hypertrophic subaortic stenosis.

b. Calcium antogonists may induce increases in plasma digoxin levels.

c. Cimetidine may increase blood levels of nifedipine.

Table 6
Adverse Drug Effects**

Drugs	Selected Side Effects#	Precautions and Special Considerations
*Diuretics**		
Thiazides and related sulfonamide diuretics	Hypokalemia, hyperuricemia, glucose intolerance, hypercholesteremia, hypertriglycerdemia, sexual dysfunction, weakness	May be ineffective in renal failure; hypokalemia increases digitalis toxicity; may precipitate acute gout; may cause an increase in blood levels of lithium
Loop diuretics	Same as for thiazides	Effective in chronic renal failure; hypokalemia and hyperuricemia as above
Potassium-sparing agents	Hyperkalemia	Danger of hyperkalemia or renal failure in patients treated with an ACE inhibitor or a nonsteroidal anti-inflammatory drug; may increase blood levels of lithium
Spironolactone	Gynecomastia, mastodynia	Interferes with digoxin immunoassay
Triamterene	———	Danger of renal calculi
Amiloride	———	———
Adrenergic Inhibitors		
Beta-adrenergic blockers+ Acebutolol Atenolol Metoprolol Nadolol Penbutolol sulfate Pindolol Propranolol hydrochloride Timolol	Bronchospasm, peripheral arterial insufficiency, fatigue, insomnia, sexual dysfunction, exacerbation of congestive heart failure, masking of symptoms of hypoglycemia, hypertriglyceridemia, decreased HDL cholesterol (except for pindolol and acebutolol)	Should not be used in patients with asthma, chronic obstructive pulmonary disease (COPD), congestive heart failure, heart block (greater than first-degree), and sick sinus syndrome; use with caution in insulin-treated diabetics and patients with peripheral vascular disease; should not be discontinued abruptly in patients with ischemic heart disease

Table 6
(continued)

Drugs	Selected Side Effects*	Precautions and Special Considerations
Centrally acting adrenergic inhibitors		
Clonidine	Drowsiness, sedation, dry mouth, fatigue, sexual dysfunction	Rebound hypertension may occur with abrupt discontinuance, particularly with prior administration of high doses or with continuation of concomitant beta-blocker therapy
Guanabenz	Same as for clonidine	Same as for clonidine
Guanfacine hydrochloride	Same as for clonidine	Same as for clonidine
Methyldopa	Same as for clonidine	May cause liver damage and Coombs-positive hemolytic anemia; use cautiously in elderly patients because of orthostatic hypotension; interferes with measurements of urinary catecholamine levels
Clonidine TTS (patch)	Same as for clonidine; localized skin reaction to the patch	———
Peripheral-acting adrenergic inhibitors		
Guanadrel sulfate	Diarrhea, sexual dysfunction, orthostatic hypotension	Use cautiously because of orthostatic hypotension
Guanethidine monosulfate	Same as for guanadrel	Same as for guanadrel
Rauwolfia alkaloids	Lethargy, nasal congestion, depression	Contraindicated in patients with history of mental depression; use with caution in patients with history of peptic ulcer
Reserpine	Same as for rauwolfia alkaloids	Same as for rauwolfia alkaloids

Table 6
(continued)

Drugs	Selected Side Effects*	Precautions and Special Considerations
Alpha-1-adrenergic blockers		
Prazosin hydrochloride	"First-dose" syncope, orthostatic hypotension, weakness, palpitations	Use cautiously in elderly patients because of orthostatic hypotension
Terazosin hydrochloride	Same as for prazosin hydrochloride	Same as for prazosin hydrochloride
Combined alpha- and beta-adrenergic blockers		
Labetalol†	Bronchospasm, peripheral vascular insufficiency, orthostatic hypotension	Should not be used in patients with asthma, COPD, congestive heart failure, heart block (greater than first-degree), and sick sinus syndrome; use with caution in insulin-treated diabetics and patients with peripheral vascular disease
Vasolidators	Headache, tachycardia, fluid retention	May precipitate angina pectoris in patients with coronary artery disease
Hydralazine	Positive antinuclear antibody test	Lupus syndrome may occur (rare at recommended doses)
Minoxidil	Hypertrichosis	May cause or aggravate pleural and pericardial effusions; may precipitate angina pectoris in patients with coronary artery disease

Table 6
(continued)

Drugs	Selected Side Effects#	Precautions and Special Considerations
ACE Inhibitors	Rash, cough, angioneurotic edema, hyperkalemia, dysgeusia	Can cause reversible, acute renal failure in patients with bilateral renal arterial stenosis or unilateral stenosis in a solitary kidney; proteinuria may occur (rare at recommended doses); hyperkalemia can develop, particularly in patients with renal insufficiency; rarely can induce neutropenia; hypotension has been observed with initiation of ACE inhibitors, especially in patients with high plasma renin activity or in those receiving diuretic therapy
Calcium Antagonists	Edema, headache	Use with caution in patients with congestive heart failure; contraindicated in patients with second- or third-degree heart block
Verapamil	Constipation	May cause liver dysfunction
Diltiazem hydrochloride	Constipation	May cause liver dysfunction
Nifedipine	Tachycardia	———
Nitrendipine	Tachycardia	———

* See Table 3 for a list of these drugs.

** Sexual dysfunction, particularly impotence in men, has been reported with the use of all antihypertensive agents.

+ Sudden withdrawal of these drugs may be hazardous in patients with heart disease. See Table 3 for a list of these drugs.

The listing of side effects is not all-inclusive, and health practitioners are urged to refer to the package insert for a more detailed listing.

Isolated Systolic Hypertension

Isolated systolic hypertension frequently occurs in the elderly and is discussed in more detail later in the "Special Populations and Management Problems" section on page 35. When isolated systolic hypertension occurs in adolescents and young adults, it often indicates a hyperdynamic circulation and may predict diastolic elevation. Initially, nonpharmacologic therapy is the preferred treatment approach for most patients with isolated systolic hypertension. However, when the systolic pressure is consistently 160 mm Hg or greater and the diastolic pressure is less than 90 mm Hg despite nonpharmacologic therapy, antihypertensive drug treatment should be considered.[35]

Moderate and Severe Hypertension

Although similar general approaches are advocated for all patients with hypertension, modification may be appropriate for those with diastolic pressures greater than 104 mm Hg. Although some patients may respond adequately to only one drug, a second agent may be prescribed after a short interval if control is not achieved. The intervals between changes in the regimen should be decreased, and the maximum dose of some drugs may be increased. Patients with average diastolic pressures of 130 mm Hg or greater require more immediate therapy and, at times, hospitalization. Physicians who are uncomfortable with treating such patients should seek consultation.

Refractory Hypertension

The treatment program outlined earlier in this report will control high blood pressure in almost all patients. However, unacceptably high diastolic blood pressures can persist in a few patients, despite combination therapy at full dose. Some of the causes of refractory hypertension are listed in Table 4. If these causes have been excluded, more potent drugs such as minoxidil may be needed. Failure to include diuretics in the antihypertensive regimen is a frequent cause of poor blood pressure control. If goal blood pressure cannot be achieved without intolerable side effects, partial reduction of diastolic blood pressure (to 90-100 mm Hg) may have to be accepted. Additional steps that may be taken include the following.

- Increase doses of drugs beyond the levels recommended in Table 3 with the realization that the likelihood of developing side effects may be increased.
- Persuade patients that they may have to tolerate some adverse effects in order to achieve goal blood pressure and to reduce the risk of morbidity and mortality.
- Measure plasma renin activity, which may at times be useful for diagnostic purposes and for selecting additional antihypertensive drugs in the patient with refractory hypertension.
- Consider referring patients for further evaluation, including assessment of secondary forms of hypertension.

Hypertensive Emergencies and Urgencies

Although not as common today as in the past, hypertensive emergencies warrant prompt recognition and management because they represent serious threats to organ function and life. Prompt initiation of therapy may reduce or prevent these threats. The association between elevated blood pressure and evidence of new or progressive end-organ damage—and not necessarily the absolute blood pressure itself—determines the seriousness of the clinical situation and the possible need for immediate treatment in a monitored hospital setting. Consultation, referral, or both should be considered when indicated.

Hypertensive emergencies are those situations in which blood pressure must be lowered within 1 hour. Examples include hypertensive encephalopathy, intracranial hemorrhage, acute left ventricular failure with pulmonary edema, dissecting aortic aneurysm, eclampsia or severe hypertension associated with pregnancy, head trauma, extensive burns, unstable angina pectoris, or acute myocardial infarction.

Hypertensive urgencies are situations in which blood pressure should be reduced within a few hours—e.g., accelerated or malignant hypertension without immediate complications and severe perioperative hypertension.

A clear distinction between emergencies and urgencies is not always possible. In these circumstances, specialized management may be appropriate from the outset. Tables 7 and 8 present those parenteral agents that have proven effective in treating hypertensive emergencies in addition to orally administered antihypertensive drugs that have been used to treat both emergencies and urgencies, including ACE inhibitors, minoxidil, clonidine, and nifedipine. Despite the benefits of timely and appropriate treatment, the possible risks of overly aggressive intervention in these circumstances must always be considered. Elevated blood pressure alone rarely requires urgent therapy.

Table 7 Parenteral Drugs for Treatment of Hypertensive Emergencies

	Dose*	Reaction Time	Adverse Reactions
Vasodilators			
Sodium nitroprusside	0.5-10 µg/kg/min as IV infusion	Instantaneous	Nausea, vomiting, muscle twitching, thiocyanate intoxication, methemoglobinemia
Nitroglycerine	5-100 µg/min as IV infusion	2-5 min	Headache, tachycardia, vomiting, methemoglobinemia
Diazoxide	50-150 mg/IV bolus, repeated, or 15-30 mg/min by IV infusion	1-2 min	Hypotension, tachycardia, aggravation of angina pectoris
Hydralazine	10-20 mg IV 10-50 mg IM	10 min 20-30 min	Tachycardia, headache, vomiting, aggravation of angina pectoris
Adrenergic Inhibitors			
Phentolamine	5-15 mg IV	1-2 min	Tachycardia, orthostatic hypotension
Trimethaphan camsylate	1-4 mg/min as IV infusion	1-5 min	Paresis of bowel and bladder, orthostatic hypotension, blurred vision, dry mouth
Labetalol	20-80 mg IV bolus every 10 min, 2 mg/min IV infusion	5-10 min	Bronchoconstriction, heart block, orthostatic hypotension
Methyldopa	250-500 mg IV infusion	30-60 min	Drowsiness

* IV indicates intravenous; IM indicates intramuscular.

Table 8 Oral Drugs for Treatment of Hypertensive Urgencies

Drug	Recommended Dose	Frequency
Captopril	25 mg	Repeat as required
Clonidine	0.1-0.2 mg	Every hour as required
Minoxidil	2.5-5 mg	Repeat after 2-3 hours
Nifedipine	10 mg	Repeat after 30 minutes

Long-Term Maintenance of Therapy

Goal

The goal of antihypertensive therapy is achievement and long-term maintenance of goal blood pressure (<140/90 mm Hg) with minimal, if any, adverse effects. Achieving hypertension control without side effects may at times require several changes in the regimen. The ultimate objective is to reduce cardiovascular morbidity and mortality.

Follow-Up Visits

Follow-up visits for reexamination and laboratory tests are indicated at intervals that may vary from a few weeks to several months depending on clinical judgment, patient adherence, adequacy of blood pressure control, and associated medical problems and abnormal test results. Patient monitoring should include blood pressure measurements in both the standing as well as the supine or sitting positions.

Clinician-Patient Interaction: Communication and Promoting Adherence to Treatment

Poor adherence to long-term treatment, both nonpharmacologic and pharmacologic, has been identified as the major reason for inadequate control of high blood pressure. Recent studies suggest that an appropriately planned program of strategies for health education intervention can significantly improve adherence to treatment, increase adequate blood pressure control, and decrease hypertension-related morbidity and mortality.[36-38] Combinations of strategies are likely to achieve the greatest improvement in long-term adherence and are usually aimed at improving understanding of the specific treatment and treatment goals, correcting misconceptions, adjusting the interventions to patients' lifestyles, and enhancing family or other social support.[38-40] The following suggestions should improve long-term adherence to antihypertensive therapy.

- Inform patients of their blood pressure level.
- Agree on a goal blood pressure.

- Be sure patients understand that high blood pressure can be controlled, but not cured; that they cannot tell their blood pressure level by the way they feel; and that they should not stop their treatment without discussing it with their physician.
- Incorporate treatment requirements into patients' daily lifestyles, to the extent possible.
- Involve patients' families in the treatment process.
- Encourage patients to self-monitor their blood pressure in selected cases.
- In selected cases, provide positive reinforcement and encouragement for achieving specific adherence goals.
- Simplify the regimen; most antihypertensive drugs can be taken twice daily, and many only once daily.
- Provide simple oral and written instructions and adequate patient information material on drug dosages, anticipated or common side effects, and therapeutic goals.
- Ask patients to state their understanding of their diagnosis and encourage them to discuss their antihypertensive medications, to report side effects, and to express problems and concerns.
- Consider using clinician-patient contracts.
- Demonstrate a willingness to modify dosages or to change drugs to avoid side effects.
- Minimize the cost of therapy.
- Increase the attention given to nonadherent patients by scheduling more frequent counseling visits.
- Contact patients if they fail to keep follow-up appointments.
- Collaborate with other health care providers such as nurses, pharmacists, nutritionists, optometrists, dentists, podiatrists, and physician assistants.

Considerations in Individual Therapy

Quality of Life

Although treatment of hypertension is a medical necessity, the impact of antihypertensive therapy on quality of life is a legitimate concern. Patients treated with various drugs sometimes experience subtle changes in emotional status, behavior, and both physical and cognitive function. Although some antihypertensive agents produce undesirable side effects more often than do other drugs, practitioners must address the impact of treatment on the quality of life for each patient. Hypertension management should be dictated by the needs and experiences of each individual.

Cost of Care

For some patients, lifelong antihypertensive care produces a burdensome financial obligation.[41] Health care providers should be aware of the total cost of care to hypertensive patients (including indirect costs such as time lost from work and transportation costs) and should try to minimize these expenses. Determinants of cost include the following.

- *Initial Workup.* Initial costs are usually for medical history, physical examination, and minimal laboratory workup. Patients with moderate or severe hypertension may require a much more extensive and expensive assessment.
- *Follow-Up Visits.* The costs of follow-up vary considerably. Frequent visits generate greater charges, but may enhance adherence to therapy and blood pressure control, thereby reducing cardiovascular sequelae. Tactics that may contain costs include monitoring blood pressure at home or relying on other community resources and nonphysician staff for such monitoring.
- *Drugs.* The selection of antihypertensive drugs influences the total cost of care. Realistic assessment of the economic impact of each drug must consider its intrinsic cost, the burden of side effects, the impact on adherence, and additional laboratory tests that may be required to monitor biochemical changes.[34] Physicians should recognize that some drugs may be priced too high for certain patients, thus diminishing their benefit by reducing adherence. In addition, some drugs that reduce the quality of life, irrespective of cost, may reduce the overall benefit of treatment by reducing adherence.

Community Programs and Health Care Systems

Most Americans have had their blood pressure measured within the last year;[42] therefore, mass screenings to detect unaware hypertensives need not be encouraged. Instead, community-based hypertension programs should increase their efforts to provide follow-up services—i.e., patient tracking efforts that complement medical management.[43] For community hypertension programs to remain effective, the direct participation of practicing physicians is essential. Community or regional high blood pressure councils can coordinate activities to ensure that disadvantaged groups are included. There should be an ongoing commitment to remove economic barriers to adequate hypertension management in all settings in which economically disadvantaged patients are served. Cooperative arrangements among voluntary and professional agencies, local health departments, and industry are encouraged. These relationships have worked well in the past, resulting in increased numbers of controlled hypertensive patients. Community hypertension programs should also develop plans and methods to evaluate their effectiveness.[44]

Hypertension treatment sites should be designed with easy access for all patients, convenient hours unique to local needs, realistic appointment scheduling to avoid prolonged waiting periods, and a staff trained in effective communication. Sites serving economically disadvantaged populations should include staff members knowledgeable in local culture and language. An ongoing effort to assess the effectiveness of hypertension control programs should be included in the program design.

Primary Prevention

Studies to determine ways to prevent hypertension are in progress. Until the results of these investigations are available, definitive recommendations cannot be made. However, data from population studies suggest that low sodium intake, weight reduction, and moderation of alcohol consumption may prevent blood pressure levels from rising. Therefore, nonpharmacologic modalities that are of value for hypertension management may be considered for primary prevention. This may particularly apply to groups at high risk for developing high blood pressure (e.g., offspring of hypertensives, blacks, obese individuals, and those with high normal blood pressure).

Special Populations and Management Problems

Black Patients

The prevalence rate of hypertension in black Americans is considerably higher than in the white population.[1] Blacks may develop hypertension at an earlier age, and the severity of hypertension in blacks is likely to be higher than that of hypertensive whites. The higher prevalence rate and greater severity of hypertension are related to the more common occurrence of strokes, end-stage renal disease, congestive heart failure, and left ventricular hypertrophy in blacks. In addition, hypertension-related death rates are disproportionately higher among blacks, particularly in younger age groups.

The potential for reduction of morbidity and mortality related to hypertension is great in blacks, and concern about high blood pressure as a health issue has prompted an increase in control efforts throughout the country. Hypertension-related death rates are declining in blacks, and stroke mortality rates in some communities have experienced greater declines in blacks than in whites. Despite these encouraging trends, hypertension continues to be the most serious health problem for black Americans.

There are no recognized differences in the responses to nonpharmacologic therapy between whites and blacks. Therefore, such approaches should be prescribed for all patients accordingly. Weight reduction is strongly indicated in obese black hypertensive patients. Such programs not only benefit elevated blood pressure levels, but also lessen the risk of diabetes mellitus, a frequent complication of obesity.

With respect to drug therapy, black hypertensive patients usually do not respond as well to beta-blockers or ACE inhibitors as do whites, and diuretics are generally more effective as monotherapy than either beta-blockers or ACE inhibitors. However, combinations of beta-blockers or ACE inhibitors with diuretics are equally effective in black and white hypertensive patients. Calcium antagonists, centrally acting alpha-adrenergic agonists, peripheral alpha-blockers, and labetalol (a combined alpha-beta-blocker) are equally effective in both groups.

Other Racial and Ethnic Minority Groups: American Indians, Asians and Pacific Islanders, and Hispanics

Little information is available to determine whether American Indians, Asians and Pacific Islanders, and Hispanics respond differently than whites to antihypertensive medications or nonpharmacologic therapy. Further studies are needed to better understand the factors influencing the control of hypertension in these groups.

Lifestyle factors are often culturally determined and may be important contributors to hypertension and its control. Therefore, clinicians who treat and counsel minority patients should pay special attention to factors such as:

- cultural diets and beliefs;
- costs of therapy;
- education and literacy level;
- language preference or barriers; and
- environmental conditions.

Elderly Patients

By 1990, an estimated 29 million people in the United States will be 65 years of age or older. Forty-five percent of this population will have a systolic blood pressure of 160 mm Hg or greater or a diastolic blood pressure of 95 mm Hg or greater. Approximately two-thirds of those over age 65 will have a systolic blood pressure of 140 mm Hg or greater or a diastolic blood pressure of 90 mm Hg or greater. Elevations of systolic or diastolic blood pressure increase the relative risk of cardiovascular morbidity and mortality at least as much for elderly patients as for younger ones.

When the onset of diastolic hypertension appears after age 55 or when hypertension in elderly patients no longer responds to a previously effective regimen, an underlying cause, usually renovascular disease, should be suspected. Efforts to identify the latter problem are particularly appropriate in view of the increased usefulness of angioplasty in the treatment of renovascular hypertension.

Data from the Veterans Administration Study,[25] the Hypertension Detection and Follow-Up Program (HDFP),[26] the Australian Trial,[27] and the European Working Party on High Blood Pressure in the Elderly (EWPHE)[45] indicate that elderly patients who have diastolic blood pressure of 90 mm Hg or greater will benefit from antihypertensive therapy. In the HDFP trial, the adherence of elderly patients to drug regimens was just as good as, if not better than, that of younger patients.[46]

No definitive data are available regarding the efficacy of antihypertensive treatment in reducing the increased risk of cardiovascular disease associated with isolated systolic hypertension. The Systolic Hypertension in the Elderly Program (SHEP)—a double-blind, placebo-controlled trial sponsored by the National Heart, Lung, and Blood Institute and the National Institute on Aging—is in progress. Until the results of this trial are available, physicians will be guided by their clinical judgment. For most elderly patients with isolated systolic hypertension, nonpharmacologic therapy seems warranted. If the decision is made to treat with drugs, systolic blood pressure should be lowered cautiously to the goal of 140-160 mm Hg.

Older patients may be more sensitive to volume depletion and sympathetic inhibition than are younger individuals because the elderly may have impaired cardiovascular reflexes that make them more susceptible to hypotension. For this reason, antihypertensive treatment should be initiated with smaller doses than usual. Increases in dosage also should be smaller and spaced at longer intervals than might be appropriate for younger patients. Drugs that have a propensity to cause orthostatic hypotension (e.g., guanethidine monosulfate, guanadrel sulfate, alpha-1-blockers, and labetalol) should be used with caution.

All antihypertensive drugs have shown efficacy in elderly patients. In the feasibility phase of the SHEP trial, diuretic therapy usually controlled isolated systolic hypertension in most patients without producing notable symptomatic side effects.[47] Calcium antagonists are effective in elderly patients as monotherapy for either diastolic or isolated systolic hypertension. Beta-blockers and ACE inhibitors also are useful as monotherapy in the elderly. Centrally and peripherally acting adrenergic inhibitors, as well as all the drugs recommended for monotherapy, are useful as step 2 drugs.

Young Patients

Less than 3 percent of children in the United States have arterial hypertension. Nonetheless, it is an important problem warranting guidelines. The *Report of the Second Task Force on Blood Pressure Control in Children—1987*[48] offers a comprehensive approach to the detection, evaluation, and treatment of high blood pressure in children. This study provides data on blood pressure distributions from more than 70,000 white, black, and Mexican-American children. Table 9 depicts the recommended classification of blood pressure levels in children, with *significant hypertension* defined as blood pressure persistently equal to or greater than the 95th percentile for age and *severe hypertension* defined as blood pressure persistently equal to or greater than the 99th percentile for age.

Table 9 Classification of Hypertension in the Young by Age Group*

	≥ 95th Percentile (mm Hg)	≥ 99th Percentile (mm Hg)
Newborns		
7 days	SBP ≥ 96	SBP ≥ 106
8-30 days	SBP ≥ 104	SBP ≥ 110
Infants	SBP ≥ 112	SBP ≥ 118
(≤ 2 years)	DBP ≥ 74	DBP≥ 82
Children	SBP ≥ 116	SBP ≥ 124
(3-5 years)	DBP ≥ 76	DBP ≥ 84
Children	SBP ≥ 122	SBP ≥ 130
(6-9 years)	DBP ≥ 78	DBP ≥ 86
Children	SBP ≥ 126	SBP ≥ 134
(10-12 years)	DBP ≥ 82	DBP ≥ 90
Children	SBP ≥ 136	SBP ≥ 144
(13-15 years)	DBP≥ 86	DBP ≥ 92
Adolescents	SBP ≥ 142	SBP ≥ 150
(16-18 years)	DBP ≥ 92	DBP ≥ 98

* Classification based on *Report of the Second Task Force on Blood Pressure Control in Children—1987.*[48]

Hypertension should not be diagnosed on the basis of a single measurement. As in adults, children require repeated measurements to determine the stability or lability of blood pressure elevation. Attention should be given to using proper equipment and technique. The widest cuff that will comfortably encircle the arm without covering the antecubital fossa should be used. For infants in whom the accuracy of measurements by auscultation is uncertain, an electronic device using a Doppler technique can be used. Whenever possible, measurements should be obtained while patients are seated in quiet, nonstressful surroundings.

The higher the blood pressure and the younger the child, the greater the possibility of secondary hypertension. A careful medical history and physical examination are essential. The laboratory tests warranted for young patients are generally similar to those recommended for adults.

The underlying cause, severity, or complications of hypertension in children will determine the degree and types of intervention required. Therapy should reduce blood pressure without causing adverse effects that limit adherence or impair normal growth and development. Nonpharmacologic interventions can be introduced as initial treatment and tailored to meet the needs of individual patients. Antihypertensive drug therapy generally should be reserved for use in patients with levels of blood pressure above the 99th percentile or with significantly elevated pressures that respond inadequately to nondrug approaches.

Pharmacologic agents generally used for adults are also effective in young persons. Uncomplicated elevated blood pressure, by itself, generally should not be a reason to restrict asymptomatic children from participating in sports and other physical activities.

Pregnant Patients

Hypertension during pregnancy may represent the syndrome of preeclampsia (pregnancy-induced hypertension) or chronic (essential) hypertension. In either situation, treatment of hypertension is beneficial in reducing both maternal and fetal mortality. Therapy instituted before pregnancy may be continued in hypertensive women who become pregnant. In women with preeclampsia, modified bed rest and proper diet may reduce the blood pressure satisfactorily. If not, antihypertensive drug therapy should begin. Methyldopa and hydralazine have been used extensively in pregnant women, but recent clinical studies indicate that beta-adrenergic blocking drugs are also effective in controlling blood pressure and improving fetal survival. ACE inhibitors have been demonstrated to increase fetal mortality in pregnant animals and should probably be avoided during pregnancy. The calcium channel blockers have proven effective in controlling severe hypertension in late pregnancy, but they could cause a decrease in uterine contractions during labor.

Surgical Candidates

Surgical patients who are adequately controlling their blood pressure with medication should be maintained on their regimen until the time of surgery, and therapy should be reinstated as soon as possible after surgery. If oral intake must be interrupted, parenteral therapy with diuretics, adrenergic inhibitors, vasodilators, sublingual nifedipine, or transdermal clonidine may be used to prevent the rebound hypertension that may follow sudden discontinuation of some of the adrenergic-inhibiting agents.

Adequate potassium supplementation should be provided to correct hypokalemia well in advance of surgery. A brief course of intravenous potassium just prior to surgery may not be sufficient to correct long-standing hypokalemia. In all cases, anesthesiologists should be informed of patients' medical status. Hypertensive patients whose blood pressure has been controlled on medication usually tolerate anesthesia better than do those whose pressures are poorly controlled.

Patients With Cerebrovascular Disease

Hypertension is the major risk factor for both thrombotic and hemorrhagic stroke. The risk of stroke is related to the level of elevated blood pressure, with systolic blood pressure more closely correlated than diastolic levels. The risk is escalated further when hypertension is present in association with smoking, heavy alcohol intake, coronary artery disease, congestive heart failure, or diabetes mellitus.

Age-adjusted mortality rates from cerebrovascular disease have decreased approximately 50 percent between 1972 and 1986. Large-scale clinical trials have demonstrated that reduction of elevated blood pressure is associated with a 30- to 50-percent decrease in incidence of both fatal and nonfatal strokes.[49] The presence of cerebrovascular disease does not contraindicate treatment of hypertension except perhaps in the early period following an acute ischemic cerebral infarction or with transient ischemic attacks. In these cases, antihypertensive therapy may be withheld temporarily to avoid critical reduction in cerebral perfusion unless the diastolic blood pressure is very high (i.e., greater than 105 mm Hg). Thereafter, the goal of therapy is to normalize blood pressure gradually and to avoid orthostatic hypotension.

An increase in blood pressure may occur in patients who have had acute stroke. Marked elevation of blood pressure associated with hemorrhagic stroke should be approached as a hypertensive emergency (see "Hypertensive Emergencies and Urgencies" section on page 29).

Patients With Coronary Artery Disease

The effect of drug treatment on the development of complications of coronary artery disease remains a critical issue in antihypertensive drug therapy. Taken as a whole, findings from clinical trials suggest that benefits of antihypertensive treatment on the incidence of either fatal or nonfatal myocardial infarction or on mortality related to coronary artery disease are modest at best. Several possible explanations have been proposed to explain these results, but this issue remains unresolved. Nevertheless, certain recommendations regarding treatment would seem appropriate.

Careful attention should be placed on the control of other cardiovascular risk factors, especially smoking, hyperlipidemia, and diabetes mellitus. For patients with mild hypertension, smoking cessation may offer as much or greater benefit as the control of high blood pressure for reducing cardiovascular risk. In addition, some studies on mild hypertension have suggested that smoking might negate any benefit from beta-blocker therapy in reducing the incidence of complications of coronary artery disease.[28]

Aggressive measures to control hyperlipidemia, including diet (and drugs if needed), should also be used.[50] In view of the findings that some antihypertensive drugs may have an adverse effect on serum lipids and lipoproteins, health practitioners should monitor serum lipids periodically. If adverse changes are observed, treatment should be altered or appropriate measures should be taken to counteract these effects.

Because of the potential adverse effects of hypokalemia and hypomagnesemia on the development of cardiac dysrhythmias, particularly in patients with coronary artery disease, therapy should include potassium supplementation or modification of antihypertensive drug treatment to prevent or correct diuretic-induced hypokalemia. With coexisting magnesium depletion, correction of potassium deficit can be difficult unless the magnesium deficiency is also managed.

Coronary artery disease is not a contraindication to the treatment of hypertension. As with patients having cerebrovascular disease, the elevated blood pressure should be reduced gradually to avoid hypotensive episodes. Beta-blockers or calcium-entry blockers may be specifically indicated because they decrease angina pectoris. In addition, for those who have had a myocardial infarction and who are at greater risk of having another event, beta-blockers may prevent or delay a subsequent myocardial infarction and reduce the risk of sudden death. Patients with ischemic heart disease do not have an increased frequency of angina pectoris or myocardial infarction when elevated blood pressures are carefully reduced. Indeed, many patients with angina pectoris note a decrease in symptoms with lowering of blood pressure and reduction of myocardial oxygen demand.

Patients With Congestive Heart Failure

Control of hypertension can improve myocardial function, prevent congestive heart failure, and lessen mortality. ACE inhibitors, when used in combination with digitalis and diuretics in patients with congestive failure (New York Heart Association class IV), have proven effective in reducing mortality due to progressive congestive heart failure. A clinical trial has also indicated that hydralazine combined with isosorbide dinitrate significantly decreases mortality in patients with less severe (classes II and III) heart failure.[51]

Patients With Left Ventricular Hypertrophy

Left ventricular hypertrophy (LVH) permits cardiac adaptation to the increased pressure and afterload imposed by elevated blood pressure. However, LVH represents a major independent risk factor for cardiac dysrhythmias and sudden death,[52] and control of elevated blood pressure should be directed toward preventing the development of LVH.

The echocardiogram provides the most sensitive and specific diagnostic evidence of cardiac involvement and enlargement, but its use is somewhat limited by cost. The electrocardiogram remains of value not only for detecting LVH but also for identifying patients who may be more predisposed to the development of cardiac dysrhythmias.

A recent area of investigative interest relates to regression of LVH. Several antihypertensive therapies appear to be effective in reducing left ventricular mass and wall thickness; these include weight loss,[53] methyldopa, beta-adrenergic blocking agents, ACE inhibitors, and calcium antagonists.[52] Diuretics also may cause reversal of hypertrophy, but not to the extent observed with these other agents. The direct-acting vasodilators minoxidil and hydralazine, which are rarely used as monotherapy, may actually increase mass.

At this time, it is not known whether reversal of hypertension-induced cardiac hypertrophy improves the independent risk of cardiovascular morbidity and mortality associated with its presence. However, evidence of LVH is an indication for intensive therapy of patients with mild hypertension.

Patients With Peripheral Vascular Disease

Hypertension is a major risk factor for the development of arteriosclerosis obliterans. As with other atherosclerosis-related complications, however, it remains uncertain whether antihypertensive therapy will favorably influence the clinical course of the disease. In some individuals with peripheral vascular insufficiency and intermittent claudication, the lowering of blood pressure can increase symptoms.

Beta-adrenergic antagonists, particularly of the nonselective type, may be contraindicated in some patients with arteriosclerosis obliterans or with Raynaud's disease since they may induce peripheral vasoconstriction. In patients with severe Raynaud's disease associated with collagen vascular diseases such as scleroderma, treatment with ACE inhibitors, with or without a calcium antagonist, may have a beneficial effect on Raynaud's disease as well as on blood pressure.

Patients With Diabetes Mellitus

Patients with hypertension and diabetes mellitus are very vulnerable to cardiovascular complications.[54] Hypertension control, as well as reduction of hyperlipoproteinemia and cessation of cigarette smoking, is particularly important in this group. Most antihypertensive therapies are effective and can be useful in diabetic patients. Many of the drugs have side effects peculiar to patients with diabetes, but none are specifically contraindicated for use in the diabetic population.

Certain drugs may impair the control of diabetes. Decreased insulin release with diuretic-induced hypokalemia is well recognized. Maintenance of the serum potassium in the normal range generally prevents much of this adverse effect. Glucose control also may deteriorate with beta-adrenergic blocking drugs.

Another problem with beta-blockers is their interference with catecholamine-induced counterregulatory responses to insulin-induced hypoglycemia. Thus, symptoms of hypoglycemia—such as palpitations, tremor, and feelings of anxiety—may be blunted, and the duration of hypoglycemia may be prolonged. Severe hypertension also can occur during hypoglycemia in diabetic patients treated with beta-blockers. Blockade of the beta-2 (vasodilatory) receptors leaves alpha- (vasoconstrictive) receptors unopposed so that both systolic and diastolic blood pressures may increase.

Neuropathic complications of diabetes are common and may influence antihypertensive drug therapy. Autonomic neuropathy with orthostatic hypotension may occur in diabetic patients and may aggravate or precipitate orthostatic hypotension.

Sexual dysfunction is also relatively common in diabetic patients and will often deteriorate further with antihypertensive drugs. Changes in therapy may be required in such patients to help maintain adherence to drug regimens.

Hyporeninemic hypoaldosteronism with resultant hyperkalemia may be seen in patients with diabetic nephropathy. Potassium-sparing diuretics, ACE inhibitors, and beta-blockers can aggravate this hyperkalemia and must be used cautiously with frequent monitoring of the serum potassium level. On the other hand, ACE inhibitors may be otherwise desirable in diabetic hypertensive patients with renal disease (see "Patients With Renal Disease" section on page 45).

Patients With Chronic Obstructive Pulmonary Disease or Bronchial Asthma

Beta-blockers may cause major, often unpredictable, bronchospasm in some patients with chronic obstructive pulmonary disease (COPD) or bronchial asthma. Therefore, beta-blockers should be avoided if possible in these patients. If no suitable alternatives are available, beta-1 selective agents and the combined alpha-beta-blocker, labetalol, may be used with caution in some patients with mild COPD and asthma.

Sympathomimetic agents are relatively contraindicated in hypertensive patients and must be used with caution. Phenylpropanolamine hydrochloride—used extensively in over-the-counter preparations (e.g., nosedrops and decongestants)—and ephedrine inhibit the hypotensive effects of guanethidine monosulfate and reserpine. Patients receiving long-term systemic corticosteroid therapy need to have their blood pressure monitored frequently to detect increases. Some drugs used for the treatment of COPD and bronchial asthma (e.g., methylxanthines, local steroid preparations, and anticholinergic nebulizers) do not significantly affect blood pressure.

Patients With Hyperlipidemia

New definitions and guidelines for the management of hypercholesterolemia and hyperlipidemia in adults are available in a recent report of an expert panel established by the National Heart, Lung, and Blood Institute.[50] Table 10 summarizes the recommended classification and treatment decisions based on total and low-density-lipoprotein (LDL) cholesterol. The report recommends treating patients earlier and taking a more aggressive approach to the control of hyperlipoproteinemia than that currently used by most physicians. In view of their importance as a risk factor, serum lipids should be monitored regularly in hypertensive patients.

Thiazide and loop diuretics can induce short-term increases in levels of total plasma cholesterol, triglyceride, and LDL in some patients.[55] Some studies have suggested that this hyperlipidemic effect decreases or disappears with long-term therapy, but several clinical trials have shown persistence of the adverse effect. Dietary modifications may reduce or eliminate these possible effects.

Beta-blockers may increase levels of plasma triglycerides and reduce high-density-lipoprotein (HDL) cholesterol levels. Despite this effect, they are the only agents that have been shown to decrease the rate of both fatal and nonfatal recurrent myocardial infarction. Beta-blockers with intrinsic sympathomimetic activity or labetalol have no adverse effect on lipids, but these agents have not demonstrated a cardioprotective effect after a myocardial infarction.

Table 10 Cholesterol Classification and Treatment Recommendations*

Risk Levels	Total Cholesterol (mg/dL)	LDL Cholesterol (mg/dL)	Action
Desirable	< 200	< 130	Remeasure within 5 years
Borderline	200-239	130-159	Without coronary artery disease or two other risk factors: provide dietary information and recheck annually
			With coronary artery disease or two or more other risk factors: an aggressive approach is indicated; dietary changes should be initiated, and drug therapy may be warranted
High	≥ 240	≥ 160	An aggressive approach is indicated; dietary changes should be initiated, and drug therapy may be warranted

* Classification based on *Report of the National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults.*[50]

The alpha-1-blockers and the central adrenergic agonists may decrease serum cholesterol concentration to a slight degree, especially in the LDL subfraction. Therefore, these agents may offer an advantage in managing hypertensive patients with hyperlipidemia. ACE inhibitors and calcium antagonists have no adverse effects on serum lipids and lipoproteins.

Patients With Gout

Thiazide diuretics may precipitate gout in susceptible patients. This is not likely to occur if gout is controlled with an agent to lower serum uric acid (e.g., allopurinol) levels or with a uricosuric drug (e.g., probenecid). For patients with poorly controlled gout, thiazide diuretics should be avoided. In the absence of gout or urate stones, diuretic-induced hyperuricemia usually does not require treatment.

Patients With Renal Disease

Antihypertensive treatment preserves renal function in severe or malignant hypertension and may decrease the degree of proteinuria or progression of renal failure in patients with primary renal disease or diabetic nephropathy. Hypertension secondary to renal parenchymal disease usually does not develop unless the serum creatinine level has risen above 1.5 mg/dL. This level corresponds to a more than 50-percent reduction in glomerular filtration rate and renal blood flow.

When renal function is impaired, sodium excretion may be compromised, leading to sodium retention and potential elevation of blood pressure. Consequently, sodium restriction and the use of diuretics are important in treatment. With marked impairment of renal function, large doses of loop diuretics (e.g., furosemide, ethacrynic acid, and bumetanide) or metolazone, instead of conventional thiazide diuretics, may be necessary to control hypertension. All of the commonly used classes of antihypertensive drugs are usually effective in lowering blood pressure in patients with renal disease and thereby may favorably influence the degree of proteinuria and the progression of renal failure. With severe hypertension, minoxidil may be needed, but increased doses of a diuretic and an antiadrenergic drug are often required to control the sodium retention and tachycardia induced by minoxidil.

Recent studies, particularly in diabetic nephropathy, suggest that the use of ACE inhibitors may possess specific advantages in decreasing proteinuria and slowing progression of renal failure. These drugs may be administered in conjunction with a diuretic or other antihypertensive drug, as necessary, to control the systemic blood pressure. When an ACE inhibitor is given to patients with an elevated serum creatinine level (i.e., greater than 2.5 mg/dL), the serum potassium level should be monitored frequently because of the increased risk for hyperkalemia. In patients with bilateral renal artery stenosis or stenosis in the artery supplying a solitary kidney, ACE inhibitors may lead to a further acute reduction in kidney function, which is usually reversible on discontinuation of the drug.

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* May be obtained from the National High Blood Pressure Education Program, 120/80, 4733 Bethesda Avenue, Suite 530, Bethesda, Maryland 20814.

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